

Application No. 09/747,521  
Amendment dated September 9, 2003 (Revised November 6, 2003)  
Reply to Office action of May 7, 2003  
Docket Number 22727/04079

## REMARKS/ARGUMENTS

Claims 23, 24, 26, 27, 31, 41, 42 and 45-50 are pending in the application. Claims 23, 24, 26, 27, 31, 41, 42 and 45-50 are rejected. By the present amendment claims 23 and 24 are amended and new claims 51-53 are added. Support for the amendments to claim 23 is found at paragraph [024], lines 1-7, paragraph [026], lines 7-11 and paragraph [0062], lines 5-8. Further support for amendment to claim 23 and amendment to claim 24 and new claims 51-53 is found at paragraph [0042], lines 5-8, paragraph [0043], lines 1-6, paragraph [0046], paragraph [0048], and Examples 1-3. The amendments and new claims add no new matter.

Figures 1A and 2A show the entire polynucleotide sequences encoding the LF and PA proteins from *B. anthracis*. The sequences shown in Figures 1A and 2A encode a full length protein which includes the signal peptides, and correspond with SEQ ID NOs 1 and 3, respectively. The amino acid sequence for the LF protein, shown in Figure 1B (shown as amino acids 1-776), corresponds with and is identical to amino acids 34-809 in SEQ ID NO 2 (a shift of 33 amino acids, which is the length of the signal peptide included in SEQ ID NO 2 but not in Figure 1B). The amino acid sequence for PA, shown in Figure 2B (shown as amino acids 1-735), corresponds with and is identical to amino acids 30-864 in SEQ ID NO 4 (a shift of 29 amino acids, which is the length of the signal peptide included in SEQ ID NO 4 but not in Figure 2B). Original Figures 1B and 2B clearly indicate that the shown amino acid sequences do not include the signal peptide sequence.

By the present amendment, the specification is corrected for clarity such that references made throughout the specification to specific amino acid sequences as shown in Figures 1B and 2B include recital of the identical and corresponding sequences shown in SEQ ID NOs 2 and 4. Specifically, where there are references to amino acid sequences 1-775 or 9-252, as shown in Figure 1B, references to the identical and corresponding amino acid sequences 34-809 or 42-285 in SEQ ID NO 2 have been added. Likewise, where there are references to amino acid sequences 1-735 or 175-735, as shown in Figure 2B, references to the identical and corresponding amino acid sequences 30-764 or 204-764 in SEQ ID NO 4 have been added. And where there are references to amino acid position 687, as shown in Figure 1B, references to the identical and corresponding amino acid position 720 in SEQ ID NO 2 have been added. Support

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for the amendments to the specification is found at paragraph [0011], Figure 1, paragraph [0021], paragraph [0040], lines 1-8 and paragraphs [0059] - [0085] (Examples 1 and 2), and original Figures 1 and 2. Accordingly, these amendments are supported by the original disclosure and do not add new matter.

Informalities in specification have also been corrected as requested by the Patent Office in paragraph [0024] to replace the term "cepteine redidue" with the term "cysteine residue", and in paragraph [0086] to replace the term "sores" with the term "spores".

Applicant thanks Examiner Shahnan Shah and her Primary Examiner, Rodney Schwartz, for the telephone interview of August 4, 2003, when enablement of the claims was discussed. Applicant especially wishes to thank the Examiners for their explanation of the enablement requirements of claims that recite an immunogenic composition or method of use verses claims that recite a composition which protects an animal receiving the same. As appropriate, Applicant has amended the claims of the present application consistent with the suggestions of the Examiners.

In view of the above-described amendments and corrections and the following remarks, reconsideration of claims 23, 24, 26, 27, 31, 41, 42 and 45-50 and consideration of new claims 51-53 are respectfully requested.

#### New Matter Objections to the Specification

Applicant submits that objections to the Specification on the basis of new matter should be withdrawn in light of the fact that the amendments made previously and currently to the claims are for the purpose of clarity, as described above, and do not involve the introduction of added material.

#### New Matter Rejections of the Claims

Applicant submits that rejection of the claims on the basis of new matter should be withdrawn in light of the fact that the amendments made previously and currently to the claims are for the purpose of clarity, as described above, and do not involve the introduction of added material. Claim 23, as previously amended recites "a mutation that eliminates the metalloproteinase activity," and as herein amended, further recites "wherein the immunogenic fragment of LF protein comprises amino acid 42 through amino acid 285 of SEQ ID NO. 2 and lacks metalloproteinase activity." Applicant submits that there is support in the original

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description for these amendments. Such support is found in paragraph [0062], which describes at lines 5-8 a mutant form of the LF protein "which contains a mutation at position 687 (E687C) in the zinc-binding active site thus eliminating the metalloproteinase activity of LF." Likewise, paragraphs [0024] and [0026] describe preferred mutants that have mutations which would eliminate the metalloproteinase activity of LF.

#### Enablement of Protective Function

Claim 23 has been amended to recite a composition which comprises a DNA plasmid. This amendment is made to clarify the form of nucleic acid which is useful for achieving insertion, replication and expression of the encoded products sufficient to produce an immune response which inactivates *B. anthracis* toxin in a mammalian subject exposed to the same. The Patent Office has suggested that a construct comprising nucleic acid in naked form is not satisfactory for use as a vaccine due to its supposed relatively poor uptake and expression in target tissue. Applicant submits that the amendments to claim 23 as recited above overcome any rejection for lack of enablement based on the form of the nucleic acid construct. In light of the foregoing, Applicant submits that amended claim 23 and its dependent claims are enabled.

#### New Claims

New claims 51-53 recite nucleic acids that are useful for achieving expression of the encoded products sufficient to produce an immune response in a mammalian subject exposed to the same. These claims are not directed to the production of a protective, or vaccine effect in the mammalian subject. Consistent with the above remarks, new claims 51-53 are believed to be enabled.

In view of the above-described amendments and remarks, it is submitted that claims 23, 24, 26, 27, 31, 41, 42 and 45-50 and new claims 51-53 are now in condition for allowance. Prompt notice of such allowance is respectfully requested.

Respectfully submitted,

Date:

Nov. 6, 2003

Diane H. Dobrea  
Diane H. Dobrea, Reg. No. 48,578  
(216) 622-8485  
Customer Number 24024

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